

## CLAIMS

We claim:

1. A targeting construct comprising:
  - 5 (a) a first polynucleotide sequence homologous to a protein phosphatase 2C gene;
  - (b) a second polynucleotide sequence homologous to the protein phosphatase 2C gene; and
  - (c) a selectable marker.
2. The targeting construct of claim 1, wherein the targeting construct further  
10 comprises a screening marker.
3. A method of producing a targeting construct, the method comprising:
  - (a) providing a first polynucleotide sequence homologous to a protein phosphatase 2C gene;
  - (b) providing a second polynucleotide sequence homologous to the protein  
15 phosphatase 2C;
  - (c) providing a selectable marker; and
  - (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.
4. A method of producing a targeting construct, the method comprising:
  - (a) providing a polynucleotide comprising a first sequence homologous to a first region of a protein phosphatase 2C gene and a second sequence homologous to a second region of a protein phosphatase 2C gene;
  - (b) inserting a positive selection marker in between the first and second sequences to form the targeting construct.  
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- 25 5. A cell comprising a disruption in a protein phosphatase 2C gene.
6. The cell of claim 5, wherein the cell is a murine cell.
7. The cell of claim 6, wherein the murine cell is an embryonic stem cell.
8. A non-human transgenic animal comprising a disruption in a protein phosphatase 2C gene.  
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9. A cell derived from the non-human transgenic animal of claim 8.

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10. A method of producing a transgenic mouse comprising a disruption in a protein phosphatase 2C gene, the method comprising:

- (a) introducing the targeting construct of claim 1 into a cell;
- (b) introducing the cell into a blastocyst;

5 (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

- (d) breeding the chimeric mouse to produce the transgenic mouse.

11. A method of identifying an agent that modulates the expression of a protein phosphatase 2C, the method comprising:

10 (a) providing a non-human transgenic animal comprising a disruption in a protein phosphatase 2C gene;

- (b) administering an agent to the non-human transgenic animal; and
- (c) determining whether the expression of protein phosphatase 2C in the non-human transgenic animal is modulated.

15 12. A method of identifying an agent that modulates the function of a protein phosphatase 2C, the method comprising:

- (a) providing a non-human transgenic animal comprising a disruption in a protein phosphatase 2C gene;
- (b) administering an agent to the non-human transgenic animal; and

20 (c) determining whether the function of the disrupted protein phosphatase 2C gene in the non-human transgenic animal is modulated.

13. A method of identifying an agent that modulates the expression of protein phosphatase 2C, the method comprising:

- (a) providing a cell comprising a disruption in a protein phosphatase 2C gene;
- (b) contacting the cell with an agent; and

25 (c) determining whether expression of the protein phosphatase 2C is modulated.

14. A method of identifying an agent that modulates the function of a protein phosphatase 2C gene, the method comprising:

- (a) providing a cell comprising a disruption in a protein phosphatase 2C gene;
- (b) contacting the cell with an agent; and

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(c) determining whether the function of the protein phosphatase 2C gene is modulated.

15. The method of claim 13 or claim 14, wherein the cell is derived from the non-human transgenic animal of claim 8.

5 16. An agent identified by the method of claim 11, claim 12, claim 13, or claim 14.

17. A transgenic mouse comprising a disruption in a protein phosphatase 2C gene, wherein the transgenic mouse exhibits at least one of the following phenotypes: a stimulus processing deficit and abnormal startle response.

18. The transgenic mouse of claim 17, wherein the stimulus processing deficit is decreased prepulse inhibition with a 90dB and 100dB prepulse.

10 19. A method of producing a transgenic mouse comprising a disruption in a protein phosphatase 2C gene, wherein the transgenic mouse exhibits at least one of the following phenotypes: a stimulus processing deficit and abnormal startle response, the method comprising:

15 (a) introducing a protein phosphatase 2C gene targeting construct into a cell;

(b) introducing the cell into a blastocyst;

(c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse comprising a disruption in a protein phosphatase 2C gene.

20 20. A cell derived from the transgenic mouse of claim 17 or claim 19.

21. A method of identifying an agent that ameliorates a phenotype associated with a disruption in a protein phosphatase 2C gene, the method comprising:

25 (a) administering an agent to a transgenic mouse comprising a disruption in a protein phosphatase 2C gene; and

(b) determining whether the agent ameliorates at least one of the following phenotypes: stimulus processing deficit and abnormal startle response.

22. A method of identifying an agent that modulates protein phosphatase 2C expression, the method comprising:

30 (a) administering an agent to the transgenic mouse comprising a disruption in a protein phosphatase 2C gene; and

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(b) determining whether the agent modulates protein phosphatase 2C expression in the transgenic mouse, wherein the agent has an effect on at least one of the following behaviors: stimulus processing and startle response.

23. A method of identifying an agent that modulates a behavior associated with a disruption in a protein phosphatase 2C gene, the method comprising:

5       (a) administering an agent to a transgenic mouse comprising a disruption in a protein phosphatase 2C gene; and

      (b) determining whether the agent modulates stimulus processing or startle response.

10      24. A method of identifying an agent that modulates protein phosphatase 2C gene function, the method comprising:

      (a) providing a cell comprising a disruption in a protein phosphatase 2C gene;

      (b) contacting the cell with an agent; and

      (c) determining whether the agent modulates protein phosphatase 2C gene function, wherein the agent modulates a phenotype associated with a disruption in a protein phosphatase 2C gene.

15      25. An agent identified by the method of claim 21, claim 22, claim 23, or claim 24.

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